Target product profiles for new antibacterial agents

Severe multidrug-resistant Gram-negative infections, antibiotic-resistant Gram-positive infections in immunosuppressed and critically ill patients, and community-acquired and health care-associated bacterial meningitis

World Health Organization

Target product profiles for new antibacterial agents

Severe multidrug-resistant Gram-negative infections, antibiotic-resistant Gram-positive infections in immunosuppressed and critically ill patients, and community-acquired and health care-associated bacterial meningitis

World Health Organization

Target product profiles for new antibacterial agents: severe multidrug-resistant Gram-negative infections, antibiotic-resistant Gram-positive infections in immunosuppressed and critically ill patients, and community-acquired and health care-associated bacterial meningitis

ISBN 978-92-4-012118-8 (electronic version)
ISBN 978-92-4-012119-5 (print version)

Suggested citation. Target product profiles for new antibacterial agents: severe multidrug-resistant Gram-negative infections, antibiotic-resistant Gram-positive infections in immunosuppressed and critically ill patients, and community-acquired and health care-associated bacterial meningitis. Geneva: World Health Organization; 2026. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at https://iris.who.int/.

Graphic design by Inis Communication

Contents

Acknowledgements

The project was led and coordinated by Valeria Gigante (Scientist, Antimicrobial Resistance Research and Development Lead, World Health Organization (WHO) Antimicrobial Resistance Division) under the supervision of Alexandra Cameron (Unit Head, WHO Antimicrobial Resistance Division). Thomas Tängdén (WHO consultant; Uppsala University, Sweden) was the lead scientific expert and prepared the scoping and draft target product profile (TPP) documents with support from Tamarie Rocke (WHO consultant, Antimicrobial Resistance Division).

WHO extends its gratitude to the Advisory Group on Research and Development for Novel Antibacterial Agents that served as the TPP development group for their valuable contributions during related virtual meetings on 18 June, 30 July and 22 September 2025, chaired by Prabhavathi Fernandes. Their insights and support have been instrumental in the development of this report.

The TPP Development Group comprised:

- Cesar A. Arias. Professor and Chief, Division of Infectious Diseases, Houston Methodist Hospital and Houston Methodist Research Institute; Department of Medicine, Weill Cornell Medical College, (United States of America); founder and scientific advisor, Molecular Genetics and Antimicrobial Resistance Unit/ International Center for Microbial Genomics, Universidad El Bosque (Colombia).
- Greg Basarab. Principal Research Officer and Associate Director, Drug Discovery and Development Centre, University of Cape Town (South Africa).
- Julia Bielicki. Professor, Paediatric Infectious Diseases Research Group at St George's University of London (United Kingdom of Great Britain and Ireland); consultant in paediatric infectious diseases and infection prevention and control, University of Basel Children's Hospital (Switzerland).
- Mark Blaskovich. Professor and Director of Translation, Centre for Superbug Solutions, Institute for Molecular Bioscience, The University of Queensland (Australia).
- Jacob Bodilsen. Clinical Associate Professor, Department of Clinical Medicine, Aalborg University Hospital (Denmark).
- Yohei Doi. Professor of Medicine and Director, Center for Innovative Antimicrobial Therapy, Fujita Health University, Japan; University of Pittsburgh (United States).
- Khalid Omar H Eljaaly. Assistant Professor, Faculty of Pharmacy, King Abdulaziz University and Hospital (Saudi Arabia).
- Habib Hasan Farooqui. Assistant Professor, College of Medicine, Qatar University (Qatar).
- Antoine Abou Fayad. Associate Professor, American University of Beirut (Lebanon).
- Prabhavathi Fernandes. Retired pharmaceutical and biotechnology executive; former chair of the National Biodefense Science Board for the Government of the United States; and former chair of the Global Antibiotic Research and Development Partnership (GARDP) Scientific Advisory Board (United States).
- Stephan Harbarth. Full Professor, Division of Infectious Control, Geneva University Hospitals and Faculty of Medicine, WHO Collaborating Centre (Switzerland).
- Sam Kariuki. Professor and Director of Drugs for Neglected Diseases initiative (DnDi), Kenya (Kenya).
- Roman Kozlov. Rector, Smolensk State Medical University, and Chief Specialist of the Ministry of Health for Clinical Microbiology and AMR (Russian Federation).
- Yin Mo. Infectious diseases physician and clinician scientist, National University Singapore (Singapore).
- Victor Musiime. Associate Professor, Department of Paediatrics and Child Health, Makerere University (Uganda).
- Norio Ohmagari. Managing Director of Disease Control and Prevention, National Center for Global Health and Medicine (Japan).
- Mical Paul. Director, Infectious Diseases Institute, Rambam Health Care Campus; Professor, The Ruth and Bruce Rappaport

Faculty of Medicine, Technion, Israel Institute of Technology (Israel).

- John H. Rex. Editor-in-Chief, AMR Solutions and Adjunct Professor of Medicine, McGovern Medical School (United States).
- Nusrat Shafiq. Professor of Clinical Pharmacology, Postgraduate Institute of Medical Education and Research (India).
- Lynn Silver. Owner, LL Silver Consulting (United States).
- Taslimarif Saiyed. CEO and Director, Centre for Cellular and Molecular Platforms (India).
- Priscilla Rupali. Senior Professor, Head of the Department of Infectious Diseases, Christian Medical College (India).
- Evelina Tacconelli. Full Professor of Infectious Diseases, University of Verona, Italy; Head of the German Center for Infection Research (DZIF) Clinical Research Unit on Healthcare Associated Infections and Antimicrobial Resistance, Tübingen University (Germany).
- Kamini Walia. Senior Scientist, Indian Council of Medical Research (India).
- Phoebe Williams. Paediatrician and Paediatric Infectious Diseases Physician, Sydney Children's Hospital; Associate Professor, Sydney Institute for Infectious Diseases, School of Public Health, Faculty of Medicine, University of Sydney (Australia).

We also acknowledge the contribution of the observers:

- Richard Alm. Chief Scientific Officer, CARB-X (United States).
- Radu Botgros. Senior Scientific Officer, European Medicines Agency (EMA), (Netherlands (Kingdom of the)).
- Vanessa Carter. WHO Antimicrobial Resistance Survivors Taskforce (United Kingdom).
- Lloyd Czaplewski. Director, Chemical Biology Ventures (United Kingdom).
- Erin Duffy. former Chief of Research & Development, CARB-X (United States).
- Teresa Chavarria-Gimenez. Policy Officer, European Commission Health Emergency and Response Authority (HERA) (Belgium).
- François Franceschi. Head of Asset Evaluation and Development and Serious Bacterial Infections Project Leader, GARDP (Switzerland).
- Inmaculada Navarro Perez. Policy Officer, European Commission Health Emergency and Response Authority (HERA) (Belgium).
- Seamus O'Brien. Head of Research and Development, GARDP (Switzerland).
- Lesley Ogilvie. Director, Global Antimicrobial Resistance R&D Hub Secretariat (Germany).
- Raquel Rodriguez. Policy Officer, European Commission Health Emergency and Response Authority (HERA) (Belgium).

WHO acknowledges the following WHO staff and consultant for their review and revision of this publication:

- Hala Amer. WHO Regional Office for the Eastern Mediterranean.
- Benedetta Allegrazzi. WHO Regional Office for the Eastern Mediterranean.
- Nicolò Binello. WHO Health Emergencies Programme.
- Ayesha De Costa. WHO Maternal, Newborn, Child and Adolescent Health, and Ageing Department.
- Janet Victoria Diaz. WHO Health Emergencies Programme.
- Georgina Humphreys, WHO consultant.
- Shaffi Fazaludeen Koya. Regional Office for the Eastern Mediterranean.
- Ali Ahmed Yahaya. WHO Regional Office for Africa.
- Benedikt Huttner. WHO Antimicrobial Resistance Division.
- Andre Ilbawi. WHO Universal Health Coverage, Communicable and Noncommunicable Diseases Division.
- Danilo Lo Fo Wong. WHO Regional Office for Europe.
- Roberta Ortiz Sequeira. WHO Universal Health Coverage, Communicable and Noncommunicable Diseases Division.
- Martina Penazzato. WHO Science Division.
- Guy Fones. WHO Universal Health Coverage, Communicable and Noncommunicable Diseases Division.
- Nathan Ford. WHO Universal Health Coverage, Communicable and Noncommunicable Diseases Division.

- Yasir Bin Nisar. WHO Maternal, Newborn, Child and Adolescent Health, and Ageing Department.
- Pilar Ramon-Pardo. WHO Regional Office for the Americas/Pan American Sanitary Bureau.
- Ajay Rangaraj. WHO Universal Health Coverage, Communicable and Noncommunicable Diseases Division.
- Lorenzo Pezzoli. WHO Health Emergencies Programme.
- Olga Tosas. WHO Antimicrobial Resistance Division.
- Takeshi Nishijima. WHO Regional Office for the Western Pacific.
- Bassim Zayed. WHO Regional Office for South-East Asia.

WHO would also like to thank all the individuals and organizations who contributed to the development of this report by providing feedback during the public consultation between 13 August and 7 September 2025.

Financial support

Funding for this report was kindly provided by the European Commission Health Emergency Preparedness and Response Authority (HERA).

The project has been funded by HERA. Its contents do not necessarily reflect the views of HERA nor of the European Union.

Abbreviations

3GCRE	third-generation cephalosporin-resistant Enterobacterales
ABSSSI	acute bacterial skin and skin structure infections
AMR	antimicrobial resistance
BL	β-lactam
BLI	β-lactamase inhibitor
BSI	bloodstream infection
CNS	central nervous system
CRAB	carbapenem-resistant *Acinetobacter baumannii*
CRE	carbapenem-resistant Enterobacterales
CRPA	carbapenem-resistant *Pseudomonas aeruginosa*
CSF	cerebrospinal fluid
HABP	hospital-acquired bacterial pneumonia
IAI	intra-abdominal infection
ICU	intensive care unit
LMICs	low- and middle-income countries
MDR	multidrug-resistant
MIC	minimum inhibitory concentration
MoA	mechanism of action
MRSA	methicillin-resistant *Staphylococcus aureus*
PD	pharmacodynamic
PK	pharmacokinetic
PPC	preferred product characteristics
R&D	research and development
TPP	target product profile
UTI	urinary tract infection
uUTI	uncomplicated urinary tract infection
VABP	ventilator-associated bacterial pneumonia
VRE	vancomycin-resistant enterococci
VREF	vancomycin-resistant *Enterococcus faecium*
WHO	World Health Organization

Terminology

In the context of public health, target product profiles (TPPs) are planning tools used to set research and development targets for manufacturers and researchers to guide the development of specific products. TPPs provide more detailed information than preferred product characteristics (PPCs) and include both minimally acceptable and preferred performance characteristics. The minimal performance characteristics should be considered a "go or no-go" decision point in the product development process. Exceptions may be considered where failure to meet a single minimal criterion is outweighed by substantial improvements in other critical areas.

By contrast, PPCs are designed to communicate unmet public health needs identified by the World Health Organization (WHO), stimulate innovation and investment in the identified areas, and communicate the desired performance and operational characteristics of health products to address those needs. The target audience for PPCs typically includes product developers including researchers, regulatory agencies, procurement agencies, and funders of research and development (R&D). PPCs are usually developed before a mature pipeline of products is available and should reflect the ideal characteristics of interventions required to achieve global health impact rapidly and effectively.

For the purposes of this report, the following definition was used for bloodstream infections (BSIs): a positive blood culture demonstrating the presence of microorganisms in the blood, often in a patient exhibiting signs of systemic infection, with contamination ruled out.

Introduction

Purpose and objectives of WHO Target Product Profiles

World Health Organization (WHO) target product profiles (TPPs) outline the desired characteristics of new target products aimed at specific diseases. They describe intended use, target populations and other key product attributes, including among others, safety, efficacy, pharmacokinetics, route of administration, stability, and access and affordability. TPPs also help frame the development of health products in alignment with global health needs and considering regulatory requirements for research and development (R&D).

> WHO TPPs for new antibacterials are intended to inform researchers, product developers, product development partnerships, regulatory agencies, procurement agencies and funders on both R&D and public health priorities. They are intended to facilitate the most expeditious development of novel antibiotics addressing the greatest and most urgent public health needs posed by antimicrobial resistance (AMR).

In the global health context, TPPs are developed when there is a commitment to accelerated product development and a need for rapid guidance. They help set R&D targets and priorities for funders and developers by defining desired performance and operational characteristics of potential new products.

The 2025 WHO TPPs for new antibacterial agents

Building on the 2020 WHO TPPs for antibacterial agents for use against enteric fever, gonorrhoea, neonatal sepsis and urinary tract infections *(1)*, the organization has developed three additional TPPs for novel antibiotics. This work includes a scoping review and prioritization of globally important clinical syndromes to be addressed by novel antibiotics.

The objectives of 2025 WHO TPPs for antibacterial agents are to:

- align antibacterial product development with the WHO bacterial priority pathogen list (BPPL) *(2),* and resistance data *(3)* with R&D priorities for novel antibacterials *(4);*
- prioritize globally relevant syndromes with high morbidity and mortality from the BPPL, including community- and hospital-acquired infections across age groups, health care settings and geographical regions;
- define quality, efficacy, safety and pharmacokinetic (PK) targets that reflect diverse patient populations, such as immunosuppressed and critically ill patients, neonates and children; and
- promote partnerships with public and private sector actors, to incentivize and de-risk antibacterial R&D.

Translating public health priorities into actionable antibacterial R&D guidance

WHO TPPs for antibacterial agents complement other efforts to guide antibacterial R&D, including the WHO BPPL *(2)*, and the periodic analysis of the antibacterial clinical and preclinical pipeline. The WHO BPPL identifies antibiotic-resistant bacterial pathogens of global public health concern based on burden, resistance and transmission patterns, among other criteria *(2)*. Building on this prioritization, WHO TPPs define the desired characteristics of new antibacterial agents within selected clinical use cases. In parallel, WHO clinical and preclinical pipeline analyses *(4)* monitor progress by assessing alignment of antibacterial candidates in development with BPPL priorities and TPP-defined needs, highlighting gaps for strategic R&D action to developers to address the most pressing public health challenges. Efforts to ensure a robust R&D pipeline need to be matched with plans for equitable access and appropriate use, which should be considered early in the product development process. This focus is essential for achieving widespread public health benefits. Once pipeline antibacterial agents are authorized and introduced into clinical use, ongoing surveillance of appropriate use through systems such as the Global Antimicrobial Resistance and Use Surveillance System (GLASS) *(5)* is essential to monitor availability, uptake, and patterns of use across settings *(3)* and other methodologies such as point prevalence surveys *(6).*

WHO bacterial priority pathogen list

The WHO BPPL prioritizes antibiotic-resistant bacterial pathogens to guide R&D as well as AMR prevention and control strategies. It is based on a systematic, evidence-based framework to assess transmission patterns and other public health determinants of bacterial pathogens representing the most urgent global public health needs *(2)*. Specifically, it includes bacterial pathogens with the highest burden of disease, mortality, transmission and resistance while considering their impacts in low- and middle-income countries (LMICs). By concentrating R&D advocacy on these priority pathogens, stakeholders can ensure that investment strategies are equitable, directed to contexts where lives are most at risk, and areas where existing treatments are failing. The prioritization of bacterial pathogens in this way underscores the urgency of aligning product development pipelines with the most pressing global health threats.

WHO clinical antibacterial pipeline analysis

Through its antibacterial clinical and preclinical agents pipeline analyses, WHO has consistently demonstrated that the pace of R&D lags behind the swift and steady evolution of bacteria, which itself is driven by widespread antibacterial use. The 2025 *Analysis of antibacterial agents in clinical and* preclinical *development (4)* revealed 90 antibacterial agents in development, with only 15 traditional antibacterial agents classified as innovative (excluding agents against *Mycobacterium tuberculosis*). Critically, few clinical candidates target BPPL pathogens, particularly metallo-β-lactamase-producing Enterobacterales, stressing the need for agents with novel mechanisms of action (MoA) *(4).* In general, antibacterial agents in the clinical pipeline combined with antibiotics approved in the past seven years are insufficient to tackle the emergence and spread of drug-resistant infections. In an ongoing effort to strategically act on AMR, global leaders emphasized that setting sound targets will be key in addressing the crisis in access and R&D of antibacterials *(7)* and called for sustained funding and collaboration between public and private sectors to drive innovation, navigate these challenges and establish global access to effective antibiotics *(8).*

Consideration for access, affordability and appropriate use

The bacterial priority pathogens targeted in the TPPs are often treated with intravenous, last-resort Reserve antibiotics according to the WHO Access, Watch and Reserve (AWaRe) classification, which may not be available and affordable in low-resource settings *(4).* New treatments for multidrug-resistant (MDR) Gram-negative bacteria, vancomycin-resistant enterococci (VRE), and bacterial meningitis caused by drug-resistant bacteria, will also mostly be Reserve antibiotics, and are therefore likely to face access barriers due to low sales volumes and high prices *(9,10).*

New antibiotics will likely require targeted efforts to ensure equitable access, with pricing strategies informed by health technology assessments and burden of disease. To ensure early and equitable access in high-risk populations, new agents should be evaluated in these groups to assess clinical relevance and enable regulatory approval. The development of oral formulations for step-down and outpatient treatments will help increase access to the new agents, especially in settings where intravenous administration is not feasible, but also poses added challenges for stewardship initiatives aiming to promote responsible use of the new medicines.

Monitoring use and resistance development for new antibiotics is needed to inform treatment decisions and guidelines *(10).* Antimicrobial stewardship guides the responsible introduction of Reserve and broad-spectrum Watch antibiotics, to ensure they are used appropriately in patients who need them and avoid excessive use that may accelerate development and spread of resistance. Stewardship should be embedded into antibiotic introduction plans through the implementation of effective antimicrobial stewardship policies and programmes, the education of health workers supported by updated guidelines, and timely access to affordable diagnostics, including susceptibility testing. These efforts should be reinforced by broader AMR strategies, such as strengthening infection prevention and control, water, sanitation and hygiene, and expanding access to effective vaccines to reduce the overall need for antibiotics *(11)*.

Other considerations relevant for all three TPPs

Early and targeted diagnostic testing in individuals with suspected infections is important to inform treatment decisions. Access to affordable, rapid and low complexity diagnostics alongside access to new treatments, promotes a rapid identification of pathogens, and antibiotic susceptibility testing allowing de-escalation and directed therapy, thereby avoiding unnecessary use of new last-resort agents. *(10).*

In addition to the targeted efficacy and safety characteristics of the new antibiotics, evidence is emerging on disruptions in the human microbiome caused by antibiotic exposure, which may have important health implications. Where possible, antibiotics with minimal impact on the microbiome should be favoured.

Scope

The TPPs focus on novel traditional antibacterial agents suitable for monotherapy; although combining the new agents with other antibiotics or non-antibiotics (e.g. enzyme inhibitors or other adjuvant therapies such as non-traditional antibacterial agents) may be considered in future development.

The appropriate design of clinical trials leading to market approval is beyond the scope of the TPPs and will ultimately be determined by regulatory agencies. It is essential that clinical trials include the patient populations, pathogens and infectious syndromes for which they are intended to be used. Since the target populations of the TPPs are often small, such as critically ill patients infected with multidrug-resistant pathogens, pragmatic and adaptive studies may have to be considered.

Patient population

The TPPs include some subpopulations of patients that would benefit from novel antibiotics and are often not eligible for participation in clinical trials, such as immunosuppressed and elderly individuals, children and neonates, as well as patients with more complicated infections. Other underrepresented patient populations (e.g. pregnant and lactating women) should also be considered in clinical development programmes and subsequent investigator-led studies. This aligns with ongoing efforts to promote timely inclusion of underrepresented populations in clinical trials and increasing alignment between the infectious diseases research community and regulators on accelerating the inclusion of pregnant women in pre-licensure clinical trials, with a goal to have PK and preliminary safety data for all new anti-infectives in pregnancy available at the time of medicine approval *(12–17)*.

WHO TPPs for new antibacterial agents

Target product profile for therapy of severe infections caused by multidrug-resistant Gram-negative bacteria

Target product profile for therapy of severe infections caused by multidrug-resistant Gram-negative bacteria

Focus: Novel antibiotics for bloodstream infections and hospital-acquired or ventilator-associated bacterial pneumonia caused by cephalosporin- and carbapenem-resistant Enterobacterales, and carbapenem-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (Table 1).

Disease burden

In the WHO 2024 BPPL, Gram-negative bacteria resistant to last-resort antibiotics are ranked among the critical- and high-priority groups, and include *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa (2)*. These pathogens are associated with high fatality in severe infections, such as complicated urinary tract infections (UTIs) and intra-abdominal infections (IAIs) associated with BSIs and hospital-acquired or ventilator-associated bacterial pneumonia (HABP/VABP), particularly among critically ill patients in intensive care units (ICUs) *(18–20).* In an analysis of the burden of AMR, carbapenem-resistant Gram-negative bacteria accounted for an estimated 216 000 attributable deaths globally in 2021 *(18).* In addition to mortality, MDR Gram-negative infections are associated with increased morbidity, prolonged hospital stays, and greater demand for intensive care, all of which strain health care systems and impact peoples' lives *(20).*

Antibiotic resistance

Multidrug resistance in Gram-negative bacteria is increasing worldwide, although the prevalence of resistance and mechanisms of resistance vary across settings and geographical areas. Acquired resistance mechanisms are often plasmid-mediated and can spread efficiently through horizontal transfer *(21).* In Enterobacterales, resistance to β-lactam antibiotics is usually mediated by β-lactamase production *(21).* Extended-spectrum β-lactamases (ESBLs) and carbapenemases are particularly concerning, as these enzymes confer resistance to broad-spectrum cephalosporins and carbapenems, included in the WHO AWaRe "Reserve" group *(10,22).* Carbapenem-resistant *A. baumannii* (CRAB) frequently harbour a combination of mechanisms, including β-lactamase production, reduced drug permeability, efflux and target site alterations *(23).* Similarly, carbapenem-resistant *P. aeruginosa* (CRPA) often carry a combination of chromosomal and acquired resistance genes that result in porin alterations, increased efflux and β-lactamase production *(20,21,24).*

Commercially available antibiotics

The main strategy to overcome enzymatic β-lactam resistance is to use combinations of a β-lactam (BL) antibiotic and a β-lactamase inhibitor (BLI) *(22,25,26).* While traditional BLIs, such as clavulanic acid, sulbactam and tazobactam, inhibit some extended-spectrum β-lactamases, they are ineffective against carbapenemases *(22–24).* Novel BLIs (e.g. avibactam and relebactam), are active against class A and class D carbapenemases, but not class B metallo-β-lactamases, which are the most prevalent enzymes in some settings *(27).* Since 2017, cefiderocol is the only newly approved antibiotic with activity against both third-generation cephalosporin-resistant and carbapenem-resistant Enterobacterales (3GCRE and CRE), CRAB and CRPA *(26).* Resistance is already emerging against the new BL/BLI combinations and cefiderocol and their use is constrained by high cost and limited registration globally *(25,28).*

The WHO Global Antimicrobial Resistance Surveillance System (GLASS) 2025 report shows that third-generation cephalosporin resistance in *E. coli* remains high globally at 44.8% (95% CI: 39.3–50.4), while *K. pneumoniae* displays an even higher global resistance of 55.2% (95% CI: 48.5–61.7). Regional variation is substantial: the African Region reports the highest levels, exceeding 70% for both pathogens (e.g. *E. coli* 70.7%, 95% CI: 62.3–78.0), whereas the European Region presents the lowest estimates (e.g. *E. coli* 19.9%, 90% CI: 15.9–24.7). *Acinetobacter* spp. show very high global carbapenem resistance, with imipenem resistance estimated at 54.3% (95% CI: 49.3–59.2). The Eastern Mediterranean Region reports the highest burden at 66.5% (95% CI: 58.1–73.9) *(3).*

Pipeline antibiotics

According to the 2025 Analysis of antibacterial agents in clinical and preclinical development *(4),* Gram-negative bacterial priority pathogens remain substantially underserved, with only five innovative agents against any of the WHO-designated critical Gram-negative pathogens: cefepime + taniborbactam, ceftibuten + ledaborbactam, OMN6, zifanocycline and BWC0977. Two of these are BL/BLI combinations, pairing a pre-existing β-lactam with a boronate BLI. Antibacterial pipeline diversity and innovation remain narrow: OMN6 is an insect host defence peptide targeting *A. baumannii*; BWC0977 is a novel pyrazino-oxazinone bacterial topoisomerase inhibitor with in vitro and in vivo activity against CRAB, CRE and CRPA; and zifanocycline is a next-generation tetracycline active against CRAB and Gram-positive multidrug-resistant pathogens including *Enterococcus faecium* and *Staphylococcus aureus (4).*

Overview of the TPP

This TPP is intended to guide the clinical development of new antibiotics for the treatment of severe infections caused by MDR Gram-negative bacteria, including complicated UTIs and IAIs associated with BSIs and HABP/VABP. To avoid overlap with the existing TPP on neonatal sepsis *(1)*, which also covers older children with infections caused by MDR Gram-negative bacteria, the present TPP does not focus on paediatric patients.

Spectrum of activity

The new treatment should ideally cover 3GCRE, CRE, CRAB and CRPA. A new agent with activity against only some MDR Gram-negative bacteria would also be valuable for targeted therapy, or as part of combination therapy in high-resistance settings. Activity against more susceptible strains of these species, and other Gram-negative pathogens, would enable the medicine to be used as empirical treatment *(29).* The development of innovative antibacterial agents for 3GCRE and CRE should be prioritized, as these organisms represent a large disease burden. There is a need for agents addressing class D β-lactamases, which predominantly contribute to carbapenem resistance in CRAB and are increasingly reported in Enterobacterales. Despite the advent of new antibiotics with activity against CRPA, investment in R&D for innovative antibacterial agents against these pathogens should continue to address their considerable burden of disease.

Key pharmacokinetic and pharmacodynamic features

The new treatment should lead to rapid clinical response (e.g. defervescence and resolution of symptoms) and microbiological response (e.g. negative cultures from blood and the site of infection). Excellent lung penetration is essential for a new drug targeting HABP/VABP. Intravenous administration is required for use in critically ill patients. Oral formulations would be used for step-down targeted therapy, and in outpatient settings where alternative options are limited. An intravenous antibiotic with once daily or less frequent dosing could be a feasible alternative for outpatient treatment, provided there are no associated safety concerns. Bioavailability and stability in the gastrointestinal tract are important considerations for the oral formulation. While the TPP focuses on systemic antibiotic treatments, inhaled antibiotics for HABP/VABP can be considered in future development.

Table 1. TPP for therapy of severe infections caused by MDR Gram-negative bacteria

	Minimal TPP	Preferred TPP
Indication for use	Severe infections, including complicated UTIs and IAIs associated with BSIs, caused by prioritized MDR Gram-negative bacteria: 3GCRE, CRE, CRAB and/or CRPA.	All criteria in the minimal TPP, including HABP/VABP.
Target population	Hospitalized patients with severe community- or hospital-acquired infection, including critically ill patients treated in ICUs.	Same as minimal TPP.

Table 1. TPP for therapy of severe infections caused by MDR Gram-negative bacteria (cont'd)

	Minimal TPP	Preferred TPP
Mechanism of action (MoA)	Any MoA is acceptable.	Novel or differentiated MoA compared to existing antibiotics.
Safety	Adverse events are reversible and can be monitored in the targeted patient population.	Same as minimal TPP, plus no need for routine therapeutic drug monitoring.
In vitro activity	Activity against prioritized MDR Gram-negative pathogens: 3GCRE, CRE, CRAB and CRPA. Low propensity for resistance development and selection.	Same as minimal TPP, plus activity against isolates with acquired resistance to new BL/BLI combinations and cefiderocol.
Efficacy	Proven clinical efficacy through randomized clinical trials in patients with Gram-negative infections, including patients with BSIs and infections caused by MDR pathogens.	Same criteria as minimal TPP, with demonstrated efficacy for HABP/VABP.
Pharmacokinetics	PK data available to support use in adult patients with severe Gram-negative infections, and optimized dosing for PK/pharmacodynamic (PD) target attainment in critically ill patients. Adequate medicine concentrations in plasma and infected tissue.	Same as minimal TPP, for HABP/VABP. Adequate medicine concentrations in epithelial lining fluid with standard or adapted dosing.
Dose regimen	1–4 times daily dosing.	1–2 times daily dosing.
Formulation/ presentation	Formulation for intravenous administration.	Formulations for intravenous and oral administration.
Route of administration	Intravenous injection or infusion.	Intravenous and oral.
Co-administration	Manageable interactions with medicines commonly used in hospitalized patients and in the ICU setting.	No interactions with drugs commonly used in hospitalized patients and in the ICU setting.
Product stability and storage	Heat-stable, two-year shelf life in hot tropical/humid climate (30°C and 65% relative humidity). Need for refrigeration (4°C) is acceptable.	Same as minimal TPP except no need for refrigeration.
Access and affordability	Dose, regimen, cost of goods and health system delivery costs should enable affordable supply and delivery and should not be a barrier to access in LMICs.	Analyses of the cost-effectiveness, affordability and acceptability from an LMIC perspective should be conducted. See section: Consideration for access, affordability and appropriate use.

Note: Minimal profile reflects the essential requirements for development, while the preferred profile outlines the ideal characteristics for broader impact and clinical utility.

WHO TPPs for new antibacterial agents

Target product profile for therapy of antibiotic-resistant Gram-positive infections in immunosuppressed and critically ill patients

Target product profile for therapy of antibiotic-resistant Gram-positive infections in immunosuppressed and critically ill patients

Focus: Novel antibiotics for severe infections, including bloodstream infections, caused by vancomycin-resistant enterococci (VRE), including vancomycin-resistant *E. faecium* (VREF) (Tables 2 and 3).

Disease burden

Immunosuppressed and critically ill patients face increased risk of severe bacterial infections. BSIs are among the leading complications in ICUs, occurring in 5–7% of ICU admissions (6 to 10 episodes per 1000 patient days) *(30,31),* contributing to morbidity and 250 000 deaths annually in North America and the European Region alone *(32,33).* Gram-positive bacteria, including the WHO high priority pathogens vancomycin-resistant *E. faecium* (VREF) and methicillin-resistant *S. aureus* (MRSA), and coagulase-negative staphylococci, are increasingly prevalent BSI pathogens, particularly in hospital-acquired infections *(34,35).* Enterococcal BSIs, especially when caused by vancomycin-resistant strains, are associated with high (25% to 50%) fatality notably higher in immunosuppressed patients, such as patients with haematologic malignancies undergoing stem cell transplantation or organ transplant recipients *(36–41).* MRSA BSI is associated with prolonged hospital stay and approximately two-fold higher mortality compared to BSI caused by methicillin-susceptible *S. aureus* (MSSA) *(42).*

Antibiotic resistance

Resistance to glycopeptide antibiotics (e.g. vancomycin and teicoplanin) in *Enterococcus* spp. involves modification of the peptidoglycan synthesis pathway, leading to reduced binding affinity to the glycopeptide target sites *(43).* This resistance mechanism is inducible and most pronounced in VanA and VanB phenotypes, which typically exhibit vancomycin minimum inhibitory concentrations (MICs) ranging from 64 to >1000 µg/L, with notable geographic variability *(44).* Most vancomycin-resistant enterococci (VRE) exhibit cross-resistance to β-lactams and aminoglycosides, which significantly limits treatment options. While a few WHO AWaRe “reserve” antibiotics, such as linezolid and daptomycin, remain available, emerging resistance to these last-resort antibiotics has been reported *(10,45,46).*

The WHO GLASS 2025 report highlights that MRSA remains a problem, with a global level of resistance in bloodstream infections of 27.1% (95% confidence interval (CI):23.5–31.0), highest in the Eastern Mediterranean Region at 50.3% (95% CI: 39.8–60.8) *(3,47).* This trend underscores the vulnerability of high-risk patients, especially in LMICs, where surveillance and diagnostic capacities are limited *(3).*

Commercially available antibiotics

Treatment of resistant Gram-positive cocci in immunocompromised and critically ill patients is challenged by drug toxicity and tolerability, interactions with other medicines, and biofilm formation *(48).* Among last-resort therapies for VRE, the essential Reserve antibiotic linezolid is hampered by interactions with other medicines (e.g. anti-depressants) and drug-induced myelosuppression, which has been reported in up to 50% of patients undergoing prolonged treatments *(49)* and is of particular concern in patients receiving anti-cancer therapy. The Reserve antibiotic daptomycin has been associated with acute eosinophilic pneumonia *(50)* and is not approved for pulmonary infections because it is inactivated by lung surfactant resulting in subtherapeutic medicine concentrations in the epithelial lining fluid *(51).* Daptomycin is approved for VRE infections by the US Food and Drug Administration (US FDA) but is not authorized for enterococcal infections by the European Medicines Agency (EMA) *(52).*

Pipeline antibiotics

Limited treatment options for severe Gram-positive infections in immunosuppressed and critically ill patients underscores the urgent need for novel agents with activity against drug-resistant pathogens, good tolerability, and minimal drug–drug interactions. Alarmingly, the 2025 WHO antibacterial pipeline analysis has underscored that only two traditional agents in the current pipeline, zifanocycline (KBP-7072) and BWC0977, report activity against both VRE and MRSA *(4).* Both agents remain in early clinical trial phase (Phase 1); typically, advancement to Phase 3 could take about 6 to 10 years *(4).*

Overview of the TPP

This TPP is intended to guide the clinical development of new antibiotics for severe Gram-positive infections, including BSIs and with a special focus on vancomycin-resistant *E. faecium*, in immunosuppressed and critically ill patients. In addition to the development of new antibiotics for adult patients, parallel or subsequent paediatric development is necessary. This includes implementation of an extrapolation plan for safety and efficacy, and considerations for oral formulations and dosing.

Spectrum of activity

The new antibiotic should cover VRE, including vancomycin-resistant *E. faecium*. Ideally, the novel agent should also be active against other antibiotic-resistant Gram-positive bacteria that cause severe infections and BSIs in the targeted patient populations, such as MRSA, methicillin-resistant coagulase-negative staphylococci and retain efficacy against more susceptible strains of these bacterial species. The preferred TPP includes activity against strains with acquired resistance to alternative last-resort treatments (i.e. linezolid- and daptomycin-resistant enterococci). A narrow-spectrum antibiotic with activity only against some Gram-positive pathogens could be used for targeted therapy, or as part of combination therapy in high-resistance settings.

Key pharmacokinetic and pharmacodynamic features

The new antibiotic should have a PK profile suitable for BSIs and other severe infections caused by enterococci, such as complicated UTIs, IAIs and bone and joint infections. A new antibiotic targeting intravascular catheter-related infections or prosthetic valve endocarditis should be active against pathogens in biofilm. Treatment with the new antibiotics should lead to rapid clinical (e.g. defervescence and resolution of symptoms) and microbiological response (e.g. negative cultures from blood and the site of infection). Intravenous administration is required for use in critically ill patients. Oral formulations would be used for step-down targeted therapy and in outpatient settings where alternative options are limited. An intravenous antibiotic with once daily or less frequent dosing could be a feasible alternative for outpatient treatment, provided there are no associated safety concerns. Bioavailability and stability in the gastrointestinal tract are important considerations for the oral formulation. While the TPP focuses on systemic antibiotic treatments, topical administration – such as local administration of antibiotics for intravascular catheter-related infections – can be considered in the future development.

Table 2. TPP for therapy of antibiotic-resistant Gram-positive infections in immunosuppressed and critically ill patients

	Minimal TPP	Preferred TPP
Indication for use	Severe infections, including BSIs, in immunosuppressed and critically ill patients, caused by antibiotic-resistant Gram-positive bacteria.	All criteria in the minimal TPP, plus more complicated infections, such as intravascular catheter-related infections and native or prosthetic valve endocarditis.
Target population	Hospitalized patients with immunosuppression and severe community- or hospital-acquired infections, including critically ill patients treated in ICUs.	Same as minimal TPP.
Mechanism of action (MoA)	Any MoA is acceptable.	Novel or differentiated MoA compared to existing antibiotics.
Safety	Adverse events are reversible and can be monitored in the targeted patient population.	Same as minimal TPP, plus no need for routine therapeutic drug monitoring.
In vitro activity	Activity against VRE, including vancomycin-resistant *E. faecium*, ideally also MRSA and methicillin-resistant coagulase-negative staphylococci. Low propensity for resistance development and selection.	Same as minimal TPP, and activity against strains with acquired resistance to linezolid and daptomycin.
Efficacy	Proven clinical efficacy in randomized controlled trials for severe Gram-positive infections, including patients with BSIs, immunosuppression, and/or infections caused by pathogens resistant to vancomycin and/or β-lactams.	Same criteria as minimal TPP and with demonstrated efficacy for more complicated infections.
Pharmacokinetics	PK data available to support use in severe Gram-positive infections in immunosuppressed patients, and optimized dosing for PK/PD target attainment in critically ill patients. Adequate medicine concentrations in plasma and in tissue of infection site.	Same criteria as minimal TPP, for more complicated infections.
Dose regimen	1–4 times daily dosing.	1–2 times daily dosing.
Formulation/ presentation	Formulation for intravenous administration.	Formulations for intravenous and oral administration.
Route of administration	Intravenous injection or infusion.	Intravenous and oral.
Co-administration	Manageable interactions with medicines commonly used in hospitalized immunosuppressed patients and in the ICU setting.	No interactions with medicines commonly used in hospitalized immunosuppressed patients and in the ICU setting.

Table 2. TPP for therapy of antibiotic-resistant Gram-positive infections in immunosuppressed and critically ill patients (cont'd)

	Minimal TPP	Preferred TPP
Product stability and storage	Heat-stable, two-year shelf life in hot tropical/humid climate (30°C and 65% relative humidity). Need for refrigeration (4°C) is acceptable.	Same as minimal TPP except no need for refrigeration.
Access and affordability	Dose, regimen, cost of goods and health system delivery costs should enable affordable supply and delivery and should not be a barrier to access in LMICs.	Analyses of the cost-effectiveness, affordability and acceptability from an LMIC perspective should be conducted. See section: Consideration for access, affordability and appropriate use.

Note: Minimal profile reflects the essential requirements for development, while the preferred profile outlines the ideal characteristics for broader impact and clinical utility.

Table 3. Special considerations for children

	Minimal TPP	Preferred TPP
Target population	Children (2–16 years old).	Neonates and infants (0–2 years old, including those born prematurely).
Efficacy and safety	When the course of infection is similar between children and adults and the product belongs to a well-established class of antibiotics, extrapolation of efficacy and safety should be applied in consultation with regulators. For first in class compounds, a risk-based approach should be considered. When the course of infection is different, safety and efficacy should be compared to standard of care in a randomized controlled trial.	Same as minimal TPP.
Pharmacokinetics	PK data available to support use in the target patient population.	Same as minimal TPP.
Formulation/ presentation	Formulation for intravenous administration.	Formulations for intravenous and oral administration. Oral formulations suitable for children, infants and neonates, e.g. functionally scored dispersible tablets and orodispersible multi-particulates (minitablets or sprinkles) or taste-masked suspensions.
Dose regimen	Weight-based dosing.	Weight-banded or age-banded dosing.

WHO TPPs for new antibacterial agents

Target product profile for therapy of community-acquired and health care-associated bacterial meningitis

Target product profile for therapy of community-acquired and health care-associated bacterial meningitis

Focus: Novel antibiotics for community-acquired meningitis caused by penicillin- and cephalosporin-resistant bacteria, and health care-associated (e.g., neurosurgical) meningitis, caused by multidrug-resistant Gram-negative bacteria and methicillin-resistant *S. aureus* (Tables 4 and 5).

Disease burden

Community-acquired bacterial meningitis is associated with high fatality and morbidity, with approximately one in six cases resulting in death and one in five individuals experiencing long-term disabilities, such as hearing loss, epilepsy or cognitive deficits *(53,54).* The majority of deaths from community-acquired bacterial meningitis are caused by *Streptococcus pneumoniae* (pneumococcus), *Neisseria meningitidis* (meningococcus), *Haemophilus influenzae*, or *Streptococcus agalactiae* (group B streptococcus, GBS). Among all-age bacterial meningitis deaths in the 2019 Global Burden of Disease Study, *S. pneumoniae* accounted for up to 18.8% of deaths, with a case fatality rate of up to 50% *(54)*. Among the neonatal population, *E. coli* and group B streptococcus are major contributors to bacterial meningitis, with *E. coli* emerging as the leading cause of death among preterm neonates *(55–59).* Despite recent improvements in patient management and prevention, including the introduction of vaccines *(60),* adjunctive dexamethasone therapy *(61),* and increased availability of antibiotics *(62),* the disease burden remains high, particularly in low-resource settings *(63,64).*

Health care-associated bacterial meningitis typically occurs following head trauma or neurological procedures, such as open surgery, ventricular drainage or insertion of cerebrospinal fluid (CSF) shunt systems. These infections are frequently caused by Gram-negative bacteria, including MDR Enterobacterales, *A. baumannii* and *P. aeruginosa,* and staphylococci, including MRSA. In the United States, the incidence of bacterial meningitis caused by nosocomial pathogens (i.e. Gram-negative bacteria and *S. aureus*), has been reported to be similar to that of meningococcus. Health care-associated bacterial meningitis is associated with high fatality and morbidity and often requires repeated surgical procedures and prolonged hospitalization. For example, 15%–29% mortality rates have been reported for Gram-negative post-neurosurgical meningitis *(65,66)*.

Antibiotic resistance

Antibiotic resistance in bacterial meningitis is an emerging medical threat, with varying epidemiology across settings and geographical regions *(65).* Empirical antibiotic treatment for community-acquired meningitis (i.e. intravenous third-generation cephalosporins), is challenged by increasing resistance in first-choice treatments resistance development in *S. pneumoniae,* one of the major drivers of community-acquired meningitis*.* Cephalosporin resistance rates have been reported to be around 18% in some Asian countries *(66)* and around 32% in children aged 0 to 5 years in Latin America and the Caribbean *(67).* Cephalosporin resistance in pneumococci is typically caused by mutations in the drug target reducing the affinity for penicillin-binding proteins, such as PBP2X and PBP1A. Empirical treatment for health care-associated bacterial meningitis (i.e. intravenous third-generation cephalosporin or carbapenem and vancomycin), is challenged by the increased prevalence of MDR Gram-negative bacteria, including 3GCRE, CRE, CRAB and CRPA, and MRSA with reduced susceptibility (MIC 2 mg/L) *(65,68,69).*

Commercially available antibiotics

Treatment for bacterial meningitis is complicated by the limited penetration of the blood–brain barrier by many available antibiotics. Empiric treatment for acute community-acquired bacterial meningitis, in both paediatric and adult populations, includes intravenous broad spectrum ceftriaxone or cefotaxime *(69).* In patients with risk factors for *Listeria monocytogenes*, combination therapy including intravenous ampicillin or amoxicillin is recommended *(69),* and the addition of intravenous vancomycin is advised in settings with high rates of penicillin- and third-generation cephalosporin-resistant *S. pneumoniae (69)*. For health care-associated bacterial meningitis, a combination of an intravenous broad-spectrum cephalosporin (or carbapenem such as meropenem) and vancomycin is typically used. Clinical and PK data are still sparse for antibiotics that demonstrate in vitro activity against carbapenem-resistant Gram-negative bacteria, including new BL/BLIs and cefiderocol *(70).*

Pipeline antibiotics

Emerging but limited evidence from case reports, PK/therapeutic drug monitoring studies and animal models supports the use of newer BL/BLI agents in treating Gram-negative central nervous system (CNS) infections, although no dedicated clinical trials have been conducted. Studies of ceftazidime + avibactam have suggested CSF penetration (most recently measured in paediatric post-neurosurgical meningitis) and successful clinical outcomes in post-neurosurgical meningitis cases *(71,72).* Cefiderocol has shown enhanced CSF penetration in a rat meningitis model (three-fold higher penetration in inflamed meninges), and several human CNS infection case series report measurable CSF concentrations and favourable outcomes, although dosing remains variable *(73).* Despite encouraging case-based and preclinical data, no Phase 2 or 3 clinical trials are currently evaluating these agents for meningitis, and their use remains off-label and investigational, underscoring the need for formal studies to guide dosing, safety and efficacy in CNS infections.

Overview of the TPP

This TPP is intended to guide the clinical development of new antibiotics for the treatment of bacterial meningitis. In addition to the development of new antibiotics for adult patients, parallel or subsequent paediatric development is encouraged. This includes implementation of an extrapolation plan for safety and efficacy, and considerations for oral formulations and dosing.

Spectrum of activity

A novel antibiotic for community-acquired bacterial meningitis should cover pathogens commonly causing these infections, including strains with acquired resistance to currently recommended empirical treatment. This would ideally include both Gram-positive bacteria (e.g. *S. pneumoniae* and group B streptococcus) and Gram-negative bacteria (e.g. *N. meningitidis*, and *H. influenzae*). A new antibiotic targeting health care-associated bacterial meningitis should ideally cover WHO priority Gram-negative bacteria, including 3GCRE, CRE, CRAB and CRPA, and staphylococci, including MRSA.

Key pharmacokinetic and pharmacodynamic features

The new antibiotics should have a PK profile suitable for meningitis (i.e. have sufficient CNS penetration to achieve therapeutic drug exposures at the infection site), and lead to rapid clinical (e.g. defervescence and resolution of symptoms) and microbiological response (e.g. negative CSF cultures). A new antibiotic targeting CSF shunt infections, a serious complication of neurosurgical CSF procedures, should be active against biofilms. Intravenous administration is required for use in critically ill patients. Oral formulations could be used for non-critically ill patients or as targeted step-down therapy, provided that the new antibiotic has the PK properties to generate reliable therapeutic drug exposures. Bioavailability and stability in the gastrointestinal tract are important considerations for the oral formulation. While the TPP focuses on systemic antibiotic treatments, topical administration, such as intraventricular administration, can be considered in the future development.

Table 4. TPP for therapy of community-acquired and health care-associated bacterial meningitis

	Minimal TPP	Preferred TPP
Indication for use	Patients with bacterial meningitis, where resistance to the current standard antibiotic treatment is suspected or proven.	All criteria included in the minimal TPP, plus infections caused by multidrug-resistant pathogens, for which there is currently no optimal treatment.
Target population	Hospitalized patients with: 1) community-acquired, or 2) health care-associated bacterial meningitis, including patients treated in ICUs.	Same criteria as minimal TPP.
Mechanism of action	Any MoA is acceptable.	Novel or differentiated MoA compared to existing antibiotics.
Safety	Adverse events are reversible and can be monitored in the targeted patient population.	Same as minimal TPP, plus no need for routine therapeutic drug monitoring.
In vitro activity	*Antibiotics for community-acquired bacterial meningitis:* Activity against pathogens commonly causing these infections with acquired resistance to current standard treatment, including pneumococci resistant to third-generation cephalosporins. *Antibiotics for health care-associated bacterial meningitis:* Activity against Gram-negative bacteria with acquired resistance to current standard treatment (including CRE, CRAB and CRPA), and/or staphylococci (including MRSA). *For both sought indications:* Low propensity for resistance development and selection.	*Antibiotics for community-acquired bacterial meningitis:* Same as minimal TPP. *Antibiotics for health care-associated bacterial meningitis:* The same criteria as minimal TPP, plus activity against strains with acquired resistance to current last-resort antibiotics, such as Gram-negative bacteria resistant to newer BL/BLIs and cefiderocol, and/or staphylococci, including MRSA, resistant to glycopeptide antibiotics.
Efficacy	Proven clinical efficacy in randomized clinical trials including patients with bacterial meningitis caused by pathogens resistant to standard treatment (see above).	Same as minimal TPP.
Pharmacokinetics	PK data available demonstrating good central nervous system (CNS) penetration to support use in patients with bacterial meningitis.	Same as minimal TPP.
Route of administration	Intravenous injection or infusion.	Intravenous and oral.
Formulation/ presentation	Formulation for intravenous administration.	Formulations for intravenous and oral administration.
Dose regimen	1–4 times daily dosing.	1–2 times daily dosing.

Table 4. TPP for therapy of community-acquired and health care-associated bacterial meningitis (cont'd)

	Minimal TPP	Preferred TPP
Co-administration	Manageable interactions with medicines commonly used in hospitalized patients and in the ICU setting.	No interactions with medicines commonly used in hospitalized patients and in the ICU setting.
Product stability and storage	Heat-stable, two-year shelf life in hot tropical/humid climate (30°C and 65% relative humidity). Need for refrigeration (4°C) is acceptable.	Same as minimal TPP except no refrigeration needed.
Access and affordability	Dose, regimen, cost of goods and health system delivery costs should enable affordable supply and delivery and should not be a barrier to access in LMIC settings.	Analyses of the cost-effectiveness, affordability and acceptability from an LMIC perspective should be conducted. See section: Consideration for access, affordability and appropriate use.

Note: Minimal profile reflects the essential requirements for development, while the preferred profile outlines the ideal characteristics for broader impact and clinical utility.

Table 5. Special considerations for children

	Minimal TPP	Preferred TPP
Target population	Children (2–16 years old).	Neonates and infants (0–2 years old, including those born prematurely).
Efficacy and safety	When the course of infection is similar between children and adults and the product belongs to a well-established class of antibiotics, extrapolation of efficacy and safety should be applied in consultation with regulators. For first in class compounds, a risk-based approach should be considered. When the course of infection is different, safety and efficacy should be compared to standard of care in a randomized controlled trial.	Same as minimal TPP.
Pharmacokinetics	PK data available to support use in the target patient population.	Same as minimal TPP.
Formulation/ presentation	Formulation for intravenous administration.	Formulations for intravenous, intramuscular and oral administration. Oral formulations suitable for children, infants and neonates (e.g. functionally scored dispersible tablets and orodispersible multi-particulates (minitablets or sprinkles) or taste-masked suspensions).
Dose regimen	Weight-based dosing.	Weight-banded or age-banded dosing.

References

1. Target product profiles for needed antibacterial agents: enteric fever, gonorrhoea, neonatal sepsis, urinary tract infections and meeting report. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/332124).
2. WHO bacterial priority pathogens list, 2024: bacterial pathogens of public health importance, to guide research, development and strategies to prevent and control antimicrobial resistance. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/376776).
3. Global antibiotic resistance surveillance report 2025: WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS). Geneva: World Health Organization; 2025 (https://iris.who.int/handle/10665/383106).
4. Analysis of antibacterial agents in clinical and preclinical development: overview and analysis 2025. Geneva: World Health Organization; 2025 (https://iris.who.int/handle/10665/382578).
5. Global Antimicrobial Resistance and Use Surveillance System (GLASS) report. Antibiotic use data for 2022. Geneva: World Health Organization; 2025 (https://iris.who.int/handle/10665/381094).
6. WHO methodology for point prevalence survey on antibiotic use in hospitals, version 1.1. Geneva: World Health Organization; 2018 (https://iris.who.int/handle/10665/280063).
7. WHO Strategic and Technical Advisory Group for Antimicrobial Resistance (STAG-AMR): report of the third meeting, 13–15 June 2023. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/374812).
8. Recommendations to address the antibiotic pipeline and access crisis in human health. Geneva: Global Leaders Group on Antimicrobial Resistance; 2024 (https://www.amrleaders.org/resources/m/item/glg-recommendations-to-address-the-antibiotic-pipeline-and-access-crisis-in-human-health).
9. Tängdén T, Carrara E, Hellou MM, Yahav D, Paul M. Introducing new antibiotics for multidrug-resistant bacteria: obstacles and the way forward. Clin Microbiol Infect. 2025;31(*3*):354–359 (https://doi.org/10.1016/j.cmi.2024.09.025).
10. AWaRe classification of antibiotics for evaluation and monitoring of use, 2023. World Health Organization, Geneva (https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.04).
11. Country preparedness for the introduction and appropriate use of antibiotics: operational guidance. Geneva: World Health Organization; 2025 (https://iris.who.int/handle/10665/381979).
12. Guidance for best practices for clinical trials. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/378782).
13. World AIDS Day 2024: calls to action [website]. Geneva: World Health Organization; 2024 (https://www.who.int/campaigns/world-aids-day/2024/calls-to-action).
14. World TB Day 2023: calls to action [website]. Geneva: World Health Organization; 2023 (https://www.who.int/campaigns/world-tb-day/2023/calls-to-action, accessed 22 September 2025).
15. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) [website]. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH); 2025 (https://www.ich.org/).
16. Moja L, Abbas M, de Kraker ME, Zanichelli V, Ombajo LA, Sharland M, et al. Reserve antibiotics: overcoming limitations of evidence generated from regulatory approval trials. Global Health. 2025;21(*1*):17 (https://doi.org/10.1186/s12992-025-01109-4).
17. 2024–2028 Strategy Putting public health needs at the centre of antibiotic drug development. Geneva: Global Antibiotic Research & Development Partnership; 2024 (https://gardp.org/gardp-strategy-2024-2028/).
18. Gandra S, Tseng KK, Arora A, Bhowmik B, Robinson ML, Panigrahi B, et al. The mortality burden of multidrug-resistant pathogens in India: A retrospective, observational study. Clin Infect Dis. 2019;69(*4*):563–570 (https://doi.org/10.1093/cid/ciy955).
19. Olaru ID, Tacconelli E, Yeung S, Ferrand RA, Stabler RA, Hopkins H, et al. The association between antimicrobial resistance and HIV infection: a systematic review and meta-analysis. Clin Microbiol Infect. 2021;27(*6*):846–853 (https://doi.org/10.1016/j.cmi.2021.03.026).
20. GBD 2021 Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. Lancet 2024;404:1199–1226 (https://doi.org/10.1016/s0140-6736(24)01867-1).

21. Lepe JA, Martinez-Martinez L. Resistance mechanisms in Gram-negative bacteria. Medicina Intens. 2022;46:392–402 (https://doi.org/10.1016/j.medine.2022.05.004).
22. Melchiorri D, Rocke T, Alm RA, Cameron AM, Gigante V. Addressing urgent priorities in antibiotic development: insights from WHO 2023 antibacterial clinical pipeline analyses. Lancet Microbe. 2025;6(*3*):100992 (https://doi.org/10.1016/j.lanmic.2024.100992).
23. Kyriakidis I, Vasileiou E, Pana ZD, Tragiannidis A. Acinetobacter baumannii antibiotic resistance mechanisms. Pathogens. 2021;10(*3*):373 (https://doi.org/10.3390/pathogens10030373).
24. Livermore DM. Of Pseudomonas, porins, pumps and carbapenems. J Antimicrob Chemother. 2001;47:247–50 (http://dx.doi.org/10.1093/jac/47.3.247).
25. Bush K. Past and present perspectives on beta-lactamases. Antimicrob Agents Chemother. 2018;62 (http://dx.doi.org/10.1128/aac.01076-18).
26. Bonomo RA. Lactamases: a focus on current challenges. Cold Spring Harb Perspect Med. 2017;7:a025239 (http://dx.doi.org/10.1101/cshperspect.a025239).
27. Yahav D, Giske CG, Gramatniece A, Abodakpi H, Tam VH, Leibovici L. New β-lactam–β-lactamase inhibitor combinations. Clin Microbiol Rev. 2020;34(*1*):e00115–20 (https://doi.org/10.1128/cmr.00115-20).
28. Manesh A, George MM, Palanikumar P, Nagaraj V, Bhanuprasad K, Krishnan R, et al. Combination Versus Monotherapy for Carbapenem-Resistant Acinetobacter Species Serious Infections: A Prospective IPTW Adjusted Cohort Study. Infect Dis Ther. 2024;13(*11*):2351–2362 (https://link.springer.com/article/10.1007/s40121-024-01042-w).
29. Jones RN. Microbial etiologies of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia. Clin Infect Dis. 2010;51 Suppl 1:S81–7 (https://doi.org/10.1086/653053).
30. Timsit JF, Ruppé E, Barbier F, Tabah A, Bassetti M. Bloodstream infections in critically ill patients: an expert statement. Intensive Care Med. 2020;46,266–284 (https://doi.org/10.1007/s00134-020-05950-6).
31. Hugonnet S, Sax H, Eggimann P, Chevrolet JC, Pittet D: Nosocomial bloodstream infection and clinical sepsis. Emerg Infect Dis. 2004;10:76–81 (https://doi.org/10.3201/eid1001.030407).
32. Viscoli C. Bloodstream infections: the peak of the iceberg. Virulence. 2016;7(*3*):248–251 (https://doi.org/10.1080/21505594.2016.1152440).
33. Marosi B, Kádár B, Bruzsa A, Kocsis L, Kamotsay K, Sinkó J, et al. Characteristics of Enterococcus species bloodstream infections among adults with and without onco-hematological malignancies: Experiences from the national center of Hungary. Eur J Microbiol Immunol. 2024;14(*2*):134–142 (https://doi.org/10.1556/1886.2024.00011).
34. Spencer R. Bacteremia caused by multi-resistant Gram-positive microorganisms. Clinical Microbiology and Infection. 1999;5(*2*):2S17–2S28 (https://doi.org/10.1111/j.1469-0691.1999.tb00538.x).
35. Ubeda C, Taur Y, Jenq RR, Equinda MJ, Son T, Samstein M, et al. Vancomycin-resistant Enterococcus domination of intestinal microbiota is enabled by antibiotic treatment in mice and precedes bloodstream invasion in humans. J. Clin. Invest. 2010;120:4332–4341 (https://doi.org/10.1172/jci43918).
36. Sangiorgio G, Calvo M, Migliorisi G, Campanile F, Stefani S. The impact of Enterococcus spp. in the immunocompromised host: A comprehensive review. Pathogens. 2024;13(*5*):409 (https://doi.org/10.3390/pathogens13050409).
37. Cattaneo C, Rieg S, Schwarzer G, Müller MC, Blümel B, Kern WV. Enterococcus faecalis bloodstream infection: Does infectious disease specialist consultation make a difference? Infection. 2021;49:1289–1297 (https://doi.org/10.1007/s15010-021-01717-3).
38. Carvalho AS, Lagana D, Catford J, Shaw D, Bak N. Bloodstream infections in neutropenic patients with haematological malignancies. Infect. Dis. Health. 2020;25:22–29 (https://doi.org/10.1016/j.idh.2019.08.006).
39. Bussini L, Rosselli Del Turco E, Pasquini Z, Scolz K, Amedeo A, Beci G, et al. Risk factors for persistent enterococcal bacteraemia: A multicentre retrospective study. J. Glob. Antimicrob. Resist. 2022;29:386–389 (https://doi.org/10.1016/j.jgar.2022.05.003).
40. Heidrich V, Bruno JS, Knebel FH, de Molla VC, Miranda-Silva W, Asprino PF, et al. Dental biofilm microbiota dysbiosis is associated with the risk of acute graft-versus-host disease after allogeneic hematopoietic stem cell transplantation. Front. Immunol. 2021;12:692225 (https://doi.org/10.3389/fimmu.2021.692225).
41. Feng D, Zhang Y-T, Qiu T-T, Xu K-L. Clinical features of infection within 100 days after hematopoietic stem cell transplantation in 313 patients with hematologic diseases. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2020;28:602–608 (https://doi.org/10.19746/j.cnki.issn.1009-2137.2020.02.041).

42. Yao Z, Wu Y, Xu H, Lei Y, Long W, Li M, Gu Y, Jiang Z, Cao C. Prevalence and clinical characteristics of methicillin-resistant Staphylococcus aureus infections among dermatology inpatients: A 7-year retrospective study at a tertiary care center in southwest China. Front Public Health. 2023;11:1124930 (https://doi.org/10.3389/fpubh.2023.1124930).
43. Courvalin P. Vancomycin resistance in G-positive cocci. Clin. Infect. Dis. 2006;42 Suppl.1:S25–S34 (https://doi.org/10.1086/491711).
44. Sujatha S, Praharaj I. Glycopeptide resistance in Gram-positive cocci: a review. Interdiscip. Perspect. Infect. Dis. 2012:10 (https://doi.org/10.1155/2012/781679).
45. Abbo L, Shukla BS, Giles A, Aragon L, Jimenez A, Camargo JF, et al. Linezolid- and vancomycin-resistant Enterococcus faecium in solid organ transplant recipients: Infection control and antimicrobial stewardship using whole genome sequencing. Clin Infect Dis. 2019;69(*2*):259–265 (https://doi.org/10.1093/cid/ciy903).
46. Rahim S, Pillai SK, Gold HS, Venkataraman L, Inglima K, Press RA, Linezolid-resistant, vancomycin-resistant Enterococcus faecium infection in patients without prior exposure to linezolid, Clin Inf Dis. 2003;36(*11*):E146–E148 (https://doi.org/10.1086/374929).
47. Bloodstream infection due to methicillin-resistant Staphylococcus aureus (MRSA) (%); Geneva: World Health Organization, Global Health Observatory; 2025. (https://www.who.int/data/gho/data/indicators/indicator-details/GHO/sdg-3.d.2-amr-infect-mrsa).
48. Gerson SL, Kaplan SL, Bruss JB, Le V, Arellano FM, Hafkin B, et al. Hematologic effects of linezolid: summary of clinical experience. Antimicrob Agents Chemother. 2002;46(*8*):2723–6 (https://doi.org/10.1128/AAC.46.8.2723-2726.2002).
49. Smith PF, Birmingham MC, Noskin GA, Meagher AK, Forrest A, Rayner CR, et al. Safety, efficacy and pharmacokinetics of linezolid for treatment of resistant Gram-positive infections in cancer patients with neutropenia. Ann Oncol. 2003;14(*5*):795–801 (https://doi.org/10.1093/annonc/mdg211).
50. Gidari A, Pallotto C, Francisci D. Daptomycin eosinophilic pneumonia, a systematic review of the literature and case series. Infection. 2024;52(*6*):2145–2168 (https://doi.org/10.1007/s15010-024-02349-z).
51. Silverman JA, Mortin LI, Vanpraagh AD, Li T, Alder J. Inhibition of daptomycin by pulmonary surfactant: in vitro modeling and clinical impact. J Infect Dis. 2005;191(*12*):2149–52 (https://doi.org/10.1086/430352).
52. Breakpoint tables for interpretation of MICs and zone diameters. Version 15.0, 2025. Basel: The European Committee on Antimicrobial Susceptibility Testing; 2025 (https://www.eucast.org/bacteria/clinical-breakpoints-and-interpretation/clinical-breakpoint-tables/).
53. Meningitis [website]. Geneva: World Health Organization; 2025 (https://www.who.int/news-room/fact-sheets/detail/meningitis).
54. GBD 2019 Meningitis Antimicrobial Resistance Collaborators. Global, regional, and national burden of meningitis and its aetiologies, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol. 2023;22(*8*):685–711 (https://doi.org/10.1016/s1474-4422(23)00195-3).
55. Schrag SJ, Farley MM, Petit S, Reingold A, Weston EJ, Pondo T, et al. Epidemiology of invasive early-onset neonatal sepsis, 2005 to 2014. Pediatrics. 2016;138:e20162013 (https://doi.org/10.1542/peds.2016-2013).
56. Stoll BJ, Puopolo KM, Hansen NI, Sánchez PJ, Bell EF, Carlo WA, et al. Early-onset neonatal sepsis 2015 to 2017, the rise of Escherichia coli, and the need for novel prevention strategies. JAMA Pediatr. 2020;174:e200593 (https://doi.org/10.1001/jamapediatrics.2020.0593).
57. Bingen E, Levy C, de la Rocque F, Boucherat M, Varon E, Alonso JM, et al. Bacterial meningitis in children: a French prospective study. Clin Infect Dis 2005;41:1059–63 (https://doi.org/10.1086/432944).
58. van de Beek D, Drake JM, Tunkel AR. Nosocomial bacterial meningitis. N Engl J Med. 2010;362:146–54 (https://doi.org/10.1056/NEJMra0804573).
59. van Ettekoven CN, Liechti FD, Brouwer MC, Bijlsma MW, van de Beek D. Global case fatality of bacterial meningitis during an 80-year period: A systematic review and meta-analysis. JAMA Netw Open. 2024;7(*8*):e2424802 (https://doi.org/10.1001/jamanetworkopen.2024.24802).
60. McIntyre PB, O'Brien KL, Greenwood B, van de Beek D. Effect of vaccines on bacterial meningitis worldwide. Lancet. 2012;380(*9854*):1703–1711 (https://doi.org/10.1016/s0140-6736(12)61187-8).
61. Vasudeva SV. Meningitis treatment and management. New York: Medscape; 2025 (https://emedicine.medscape.com/article/232915-treatment).
62. Bodilsen J, D'Alessandris QG, Humphreys H, Iro MA, Klein M, Last K, et al; ESCMID Study Group for Infections of the Brain (ESGIB). European Society of Clinical Microbiology and Infectious Diseases guidelines on diagnosis and treatment of brain abscess in children and adults. Clin Microbiol Infect. 2024;30(*1*):66–89 (https://doi.org/10.1016/j.cmi.2023.08.016).

63. Meningitis [website]. Geneva: World Health Organization; 2025 (https://www.who.int/health-topics/meningitis).
64. Scarborough M, Thwaites GE. The diagnosis and management of acute bacterial meningitis in resource-poor settings. Lancet Neurol. 2008;7(*7*):637–48 (https://doi.org/10.1016/s1474-4422(08)70139-x).
65. Huang N, Jia H, Zhou B, Zhou C, Cao J, Liao W, et al. Hypervirulent carbapenem-resistant Klebsiella pneumoniae causing highly fatal meningitis in southeastern China. Front Public Health. 2022;10:991306 (https://doi.org/10.3389/fpubh.2022.991306).
66. Wang CY, Chen YH, Fang C, Zhou MM, Xu HM, Jing CM, et al. Antibiotic resistance profiles and multidrug resistance patterns of Streptococcus pneumoniae in pediatrics: A multicenter retrospective study in mainland China. Medicine (Baltimore). 2019;98(*24*):e15942 (https://doi.org/10.1097/md.0000000000015942).
67. Sandoval MM, Ruvinsky S, Palermo MC, Alconada T, Brizuela ME, Wierzbicki ER, et al. Antimicrobial resistance of Streptococcus pneumoniae from invasive pneumococcal diseases in Latin American countries: a systematic review and meta-analysis. Front Public Health. 2024 Jan 22;12:1337276 (https://doi.org/10.3389/fpubh.2024.1337276).
68. Lignieres G, Rybak A, Levy C, Birgy A, Bechet S, Bonacorsi S, et al. Meningitis caused by extended-spectrum β-lactamase-producing Escherichia coli in infants in France: a case series. JAC Antimicrob Resist. 2023;5(*2*):dlad042 (https://doi.org/10.1093/jacamr/dlad042).
69. WHO guidelines on meningitis diagnosis, treatment and care. Geneva: World Health Organization; 2025 (https://iris.who.int/handle/10665/381006).
70. Hsu AJ, Chiotos K, Heil EL, Shields RK, Tamma PD. The effectiveness of newer beta-lactams for the treatment of antimicrobial-resistant Gram-negative meningitis. Clin Infect Dis. 2025;80(*5*):959–968 (https://doi.org/10.1093/cid/ciaf071).
71. Ren J, Wang Q, Liu L, Xiao Y, Ji P, Du H, et al. Ceftazidime-avibactam treatment for severe post-neurosurgical meningitis and abscess caused by extended-spectrum β-lactamase Escherichia coli in a pediatric patient: a case report. Infect Drug Resist. 2023;16:1905–1911 (https://doi.org/10.2147/IDR.S403527).
72. Gatti M, Virgili G, Cojutti PG, Gaibani P, Conti M, Sturiale C, et al. Real-time optimization of pharmacodynamic target attainment at infection site during treatment of post-neurosurgical ventriculitis caused by carbapenem-resistant gram negatives with ceftazidime–avibactam-based regimens: a report of two cases. Microorganisms. 2022;10(*1*):154 (https://doi.org/10.3390/microorganisms10010154).
73. Takemura M, Kanazawa S, Kohira N, Aoe Y, Morimoto A, Horiuchi K, Inoue Y, Yamano Y. 1106. Evaluation of penetration of cefiderocol into cerebrospinal fluid using a rat meningitis model. Open Forum Infect Dis. 2021;8(Suppl 1):645 (https://doi.org/10.1093/ofid/ofab466.1300).

(All references were accessed on 10 November 2025).

Annex 1. Overview of TPP development process

To prioritize the clinical syndromes for three new global health target product profiles (TPPs), a modified Delphi approach *(1)* was chosen while following the standardized WHO TPP development process, a methodology that comprises eight main steps (see Fig. A1).

Step 1. Identification of the need for TPPs

The WHO Secretariat started to determine if a WHO TPP or PPC were needed according to the most urgent unmet public health need. The decision to develop TPPs rather than preferred product characteristics (PPCs) was driven by the maturity of the evidence base, the urgency of the public health need, and the strategic objective of providing clear, actionable guidance to developers. The Secretariat was guided by the Director-General's report to the 78th World Health Assembly (2025) *(2)* and the 2024 *WHO bacterial priority pathogens list* (BPPL) *(3)* (Fig. A2), which both clearly define public health priorities to guide TPP development.

A literature review was conducted alongside an analysis of the antibacterial pipeline (2024–2025), confirming gaps in product development. Consultations with the WHO Technical Advisory Group on the Research and Development of Antibacterial Agents and external stakeholders validated the demand for WHO-led guidance. The TPP Development Group ultimately comprised experts in infectious diseases, antibiotic research and development (R&D), clinical microbiology, antibiotic regulation, and antimicrobial resistance (AMR) research. An extended bibliography arising from the literature review is presented in Annex 3.

Fig. A1. Outline of TPP development process

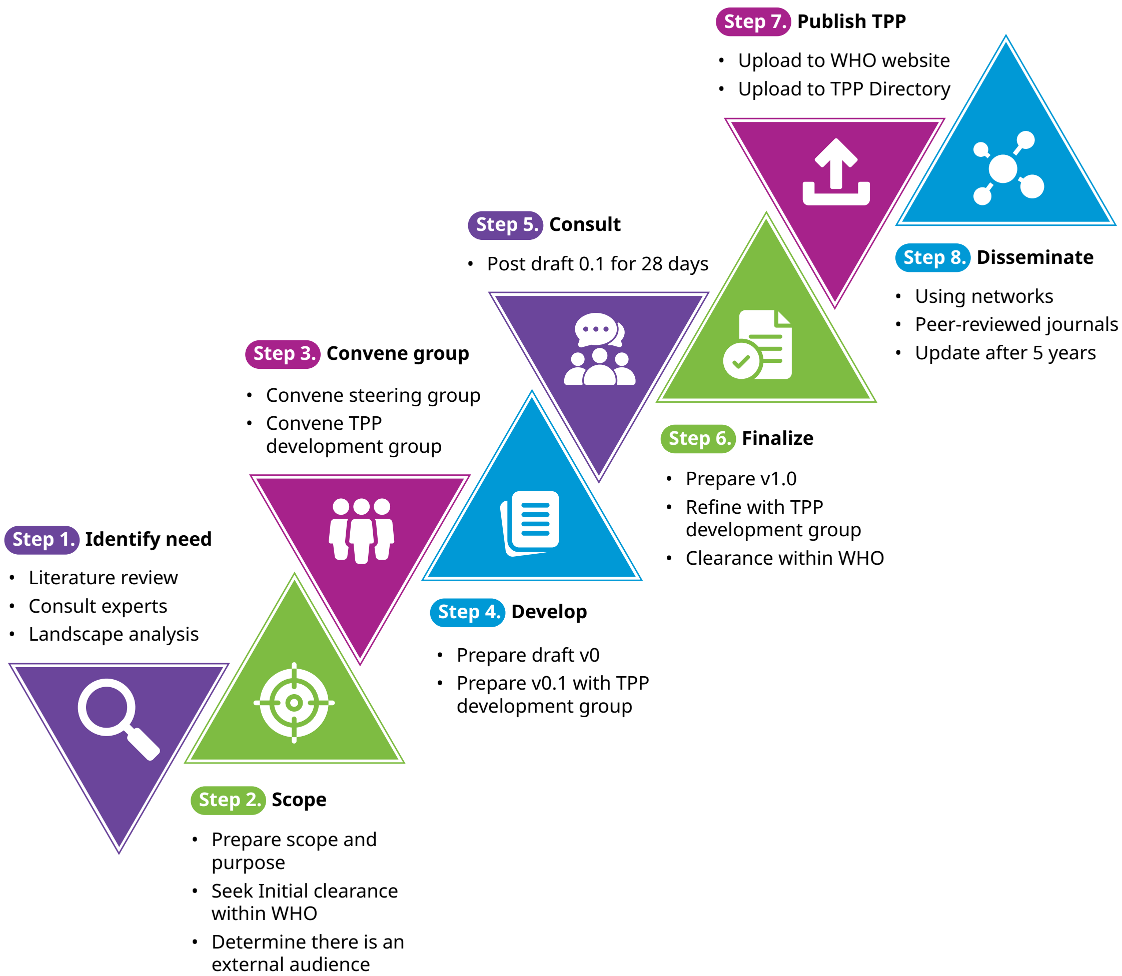

Fig. A2. WHO bacterial priority pathogen list, 2024

Step 2. Definition of scope and purpose

The TPPs were scoped to target bacterial pathogens listed in the 2024 WHO BPPL *(3)*. Two survey rounds and expert group meetings informed the prioritization of clinical syndromes. Criteria for prioritization included unmet medical needs across any of the six WHO regions, and scarcity of novel products to meet these medical needs in the antibacterial R&D pipeline. The WHO Secretariat also explored the need to stimulate innovation in less common indications such as typhoid and sexually transmitted infections, extending the scope beyond typical targets such as complicated urinary tract infections (cUTIs), community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSIs). Conditions outside those given by pathogens on the BPPL and those under the remit of other WHO departments, such as rifampicin-resistant tuberculosis (RR-TB), were excluded from scope.

Step 3. Convene steering and TPP development group

A WHO TPP Steering Group, supported by the WHO Secretariat, was established with a designated WHO technical officer to guide the process. The WHO TPP Development Group, drawing on the expertise of the WHO Advisory Group on R&D for Novel Antibacterials, ensured alignment with WHO mandates and oversaw prioritization, development and revision of the TPPs.

Following the prioritization phase, relevant staff from other WHO departments and programmes were integrated into the TPP Development Group including staff from the World Health Emergency Programme, the Maternal, Child and Adolescent Health Department, the Office of the Chief Scientist, HIV Department, Noncommunicable Disease Department, among others.

Step 4. Development of the TPPs

The WHO TPP Steering Group prepared the initial draft of the TPP (Version 0). This draft was refined into Version 0.1 after subsequent revisions from members of the Steering Group. Version 0.1 was then shared with the TPP Development Group. The three draft TPPs were developed with improved clarity and alignment with the intended objectives. This version included a comprehensive background section covering: disease burden; antibiotic resistance; available treatment options; therapies in development; the purpose of the TPP; considerations for access and affordability; and special consideration for paediatric development. Key product characteristics were outlined in a structured table format, detailing both minimal and preferred requirements. These characteristics included: indication for use; target population; mechanism of action; access and affordability; safety; in vitro activity; clinical efficacy; formulation and presentation; dosing regimen; route of administration; product stability and storage; pharmacokinetics; and consideration for co-administration.

Step 5: Invitation for public comments

On 13 August 2025, the draft TPPs were published online with an invitation for public comment until 7 September 2025, in line with WHO guidance requiring a minimum 14-day consultation period. A digital form was made available on a WHO-secure platform to facilitate structured feedback. All submissions were collated, reviewed, and analysed by the WHO TPP Steering Group. Key issues were then discussed in the third and final meeting with the TPP Development Group, held on 22 September 2025.

Step 6. Finalization of the TPP

Following review of public comments and TPP Development Group feedback, revised drafts were finalized as Version 1.0. The TPP Development Group endorsed the final content, and the WHO Secretariat ensured alignment with WHO standards for publication and dissemination.

Step 7. Publication of the TPP

The final target product profiles and meeting report is being published on the WHO website as official guidance. The TPPs will be also published on the WHO TPP directory (https://www.who.int/tools/target-product-profile-database).

Step 8. Dissemination of TPPs

To ensure broad accessibility and visibility, the finalized TPPs were submitted to the WHO TPP directory (see above) and widely disseminated, particularly among stakeholders involved in WHO policy development. Dissemination efforts were stakeholder-focused and included activities such as an official WHO press release, scientific conference presentations and webinars. Additionally, publication in a peer-reviewed journal was considered to further enhance visibility and accelerate uptake among relevant stakeholder groups.

Next steps: recommendation for future TPP and timeframe

During the TPPs development process, the WHO Technical Advisory Group on the Research and Development of Antibacterial Agents recommended updating the TPP on the treatment of neonatal sepsis, including its expansion to address sepsis in older children. They also recommended an update to the TPP for the treatment of bacterial gastroenteritis caused by drug-resistant *Salmonella* spp. including also drug-resistant *Shigella* spp. The WHO TPPs should be updated every 5 years.

References

1. Dalkey N, Helmer O. An Experimental application of the DELPHI method to the use of experts. Management Science 1963 9:3, 458–467 (http://www.jstor.org/stable/2627117).
2. Antimicrobial resistance. Report by the Director-General. Geneva: World Health Organization; 2025 (https://apps.who.int/gb/ebwha/pdf_files/WHA78/A78_8-en.pdf).
3. WHO bacterial priority pathogens list, 2024: bacterial pathogens of public health importance, to guide research, development and strategies to prevent and control antimicrobial resistance. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/376776).

(All references were accessed on 10 November 2025).

Annex 2. Declaration of interests of TPP Development Group members

Management of conflicts of interest was a priority throughout the analysis and decision-making for the TPPs. The declarations of interest (DOIs) were collected and thoroughly reviewed by the WHO AMR Division following WHO standard operating procedures.

Prior to the TPP Development Group meeting, all experts submitted written disclosures of competing interests that had arisen during a period of four preceding years and that were relevant for consideration before their confirmation as participants in the meeting, including employment by a commercial entity, consultancy, board or advisory board membership, lecture fees, expert witness income, industry-sponsored grants (including contracted research, patents received or pending, royalties, stock ownership or options), other personal financial interests, as well as whether the institution or employer had a financial relationship with a commercial entity that had an interest in the potential antibacterial products evaluated by the advisory group.

Experts were also asked to disclose academic or scientific activities that included leadership of research or grant applications, in either primary clinical studies or reviews, directly bearing on a the work/decisions of the group. In addition, at the start of the meeting, all members were asked to provide updates about their declaration if any new conflicts had arisen in the meantime.

The experts who declared no perceived conflicts of interest were Antoine Abou Fayad, Julia Anna Bielicki, Jacob Bodilsen, Khalid Eljaaly, Habib Hasan Farooqui, Prabha Fernandes, Stephan Harbarth, Sam Kariuki, Roman Kozlov, Christian Lienhardt, Norio Ohmagari, Priscilla Rupali, Taslimarif Saiyed, Nusrat Shafiq, Melvin Spigelman, Phoebe Williams and Victor Musiime. These experts were allowed full participation in the meeting.

The experts who disclosed conflicts of interest were Cesar Arias, Greg Basarab, Mark Blaskovich, Yohei Doi, Mical Paul, John Rex, Taslimarif Saiyed, Lynn Silver, and Mo Yin.

Cesar Arias declared royalties from a book chapter related to enterococcal infections.

Greg Basarab disclosed having provided consulting services to Arrepath Inc., CARB-X, and Enable 2. He also disclosed serving in the Scientific Advisory Board (SAB) of the Grand Challenges African Drug Discovery Accelerator, and GARDP.

Mark Blaskovich reported having provided consultancy in the previous 4 years to Lixa (SAB). He also declared honoraria for presentations on antimicrobial agents/antibiotic research by Pfizer Australia.

Yohei Doi reported having provided consultancy in the previous 4 years to Shionogi, GSK, Meiji Seika Pharma, Moderna, Pfizer, and AbbVie being part of their Scientific Advisory Board (SAB).

Mical Paul disclosed currently having received research support to her institution from Shionogi.

John H. Rex disclosed having provided consulting services, received research grants/support, held shares or commercial interest in Advent Life Science, Basilea Pharmaceutica (SAB), Bugworks Research Inc. (SAB), and AMR Action Fund (SAB). He also declared shares from AstraZeneca Pharmaceuticals, F2G, and Advent Life Sciences.

Taslimarif Saiyed reported being Director at RapidDx, an Indian Diagnostics Company.

Lynn Silver reported having provided consultancy, reviewed programmes or grants for Forge/Blacksmith, IOI/Germinate, Novo-Repair Fund, AMED-Japan, ENABLE I and II, NIH, Uppsala, EU GNA NOW, IMI2, Dartmouth and Notre Dame.

Mo Yin reported having received research support from Pfizer.

Following assessment of the DOIs, Cesar Arias, Greg Basarab, Mark Blaskovich, Yohei Doi, John Rex, Lynn Silver, and Mo Yin were granted participation in meetings, where their conflicts were disclosed and accounted for.

After having consulted the WHO Compliance, Risk Management and Ethics Office, Lloyd Czaplewski was invited as an observer. He disclosed that he provided consultancies to Clarametyx, Novo Repair Impact Fund, Novo Holdings, and Curza. He also declared a brief indirect consultancy in 2021 now ended with a tobacco company interested in diversifying interests including antibacterial therapies.

The following participants were invited as observers: no DoI was formally reviewed and they were granted full participation under the WHO rules of procedures governing Advisory Group meetings: Richard Alm, Radu Botgros, Vanessa Carter, Teresa Chavarria-Gimenez, Erin Duffy, François Franceschi, Inmaculada Navarro Perez, Seamus O'Brien, Lesley Ogilvie and Raquel Rodriguez.

All reported interests were disclosed to the meeting participants by the WHO technical unit in a slide show presentation. The interests disclosed in this report will also be disclosed in subsequent relevant publications.

Annex 3. Further reading

1. GLASS method for estimating attributable mortality of antimicrobial resistant bloodstream infections. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/332457).
2. Target product profile for diagnostics to detect neonatal sepsis and possible serious bacterial infection. Draft for public consultation. Geneva: World Health Organization; 2025 (https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/amr-spc-sel-glass/neonatal-sepsis-test-tpp-v0.1-draft-for-public-consultation-20240614.pdf).
3. Target product profile – Therapeutic Product (Gram-negative lower respiratory infections). Boston: Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) Publications; 2022 (https://carb-x.org/target-product-profiles/https://carb-x.org/wp-content/uploads/2025/03/2025-Tx-TPPs-and-MEC.pdf).
4. Target product profiles for needed antibacterial agents: enteric fever, gonorrhoea, neonatal sepsis, urinary tract infections and meeting report. Geneva: Global Antibiotic R&D Partnership; 2020 (https://revive.gardp.org/resources/target-product-profiles/).
5. BARDA Target Product Profiles (TPP). Planning tools for therapeutic, vaccine, and diagnostic and device candidates. Washington, DC: Biomedical Advanced Research and Development Authority (BARDA) (https://www.medicalcountermeasures.gov/barda/tpps/https://medicalcountermeasures.gov/barda/tpp).
6. Target product profile directory. Geneva: World Health Organization; 2025 (https://www.who.int/tools/target-product-profile-database).
7. https://doi.org/10.1016/S0140-6736(24)00495-1 Poggi C, Dani C. New antimicrobials for the treatment of neonatal sepsis caused by multi-drug resistant bacteria: a systematic review. Antibiotics (Basel). 2023;12(*6*):956 (https://doi.org/10.3390/antibiotics12060956).
8. Thomson KM, Dyer C, Liu F, Sands K, Portal E, Carvalho MJ, et al. BARNARDS Group. Effects of antibiotic resistance, drug target attainment, bacterial pathogenicity and affordability on outcomes in neonatal sepsis: a prospective substudy. Lancet Infect Dis. 2021;21(*8*):1231–1240 (https://doi.org/10.1016/S1473-3099(21)00050-5).
9. Dermitzaki N, Balomenou F, Serbis A, Atzemoglou N, Giaprou L, Baltogianni M, Giapros V. Multi-drug resistant Gram-negative sepsis in neonates: The special role of ceftazidime/avibactam and ceftolozane/tazobactam. Medicines (Basel). 2025;12(*3*):17 (https://doi.org/10.3390/medicines12030017).
10. Mahmood S, et al. Mecillinam activity against multidrug-resistant Shigella sonnei: a potential oral therapy. Microbiol Spectr. 2024;12(*4*):e01006–24 (https://doi.org/10.1128/spectrum.01006-24).
11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10672068/https://doi.org/10.1038/s41598-025-91340-1https://doi.org/10.1371/journal.pone.0290639 Sivanandy P, Manirajan P, Ooi WQ, Teng Khai O, Chun Wei O, Wei Ying N, et al. A systematic review of efficacy and safety of newer drugs approved from 2016 to 2023 for the treatment of complicated urinary tract infections. Ann Med. 2024;56(*1*):2403724 (https://doi.org/10.1080/07853890.2024.2403724).
12. Johansson L, et al. Daily fosfomycin versus levofloxacin for step-down therapy in complicated UTIs: randomized clinical study. mBio. 2023;14(*3*):e01677-23 (https://doi.org/10.1128/mBio.01677-23).
13. https://doi.10.3390/microorganisms13050963 Frontiers Editorial Board. New insights in prosthetic joint infections: antibiotic strategies for biofilm eradication. Front Microbiol. 2024;15:1522400 (https://doi.org/10.3389/fmicb.2024.1522400).
14. https://doi.org/10.1128/aac.00655-24https://doi.org/10.3390/antibiotics12061072https://doi.org/10.3390/antibiotics13040293 Bell C. How to save 400,000 babies a year – NeoTest AMC explained. Vox. 14 May 2025 [website] (https://www.vox.com/future-perfect/412847/neonatal-sepsis-infant-death-foreign-aid-test).
15. Wen S, Ezure Y, Rolley L, Spurling G, Lau CL, Riaz S, et al. Gram-negative neonatal sepsis in low- and lower-middle-income countries: systematic review and meta-analysis. PLoS Med. 2021;18(*9*):e1003787 (https://doi.org/10.1371/journal.pmed.1003787).
16. Flannery DD, Chiotos K, Gerber JS, Puopolo KM. Neonatal multidrug-resistant gram-negative infection: epidemiology, mechanisms of resistance, and management. Pediatr Res. 2022;91(*2*):380–391 (https://doi.org/10.1038/s41390-021-01745-7).

17. Sokou R, Filippatos F, Daniil V, Bikouli ED, Tsantes AG, Piovani D, et al. Group A streptococcus infection in neonatal population: a systematic review of the literature. J Clin Med. 2023;12(*22*):6974 (https://doi.org/10.3390/jcm12226974).
18. Zhu M, Lin J, Zhuge Z, Zheng Y, Ye S, Wang X, et al. Pathogen distribution of neonatal bacterial meningitis in the era of multidrug-resistant bacteria: a single-center experience. Infect Drug Resist. 202427;17:5277–5286 (https://doi.org/10.2147/IDR.S487757).
19. Wondimu MN, Toni AT, Zamanuel TG. Magnitude of neonatal meningitis and associated factors among newborns with neonatal sepsis admitted to the University of Gondar Comprehensive Specialized Hospital, North Gondar, Ethiopia. PLoS One. 2023;18(*9*):e0290639 (https://doi.org/10.1371/journal.pone.0290639).
20. Turner PJ, Fanshawe TR, Freeman J, et alplaTform fOr Urinary tract infection diagnostiC evAluatioN (TOUCAN): a protocol for a prospective diagnostic accuracy study of point-of-care testing in patients suspected of acute uncomplicated urinary tract infection in primary care clinics in England. BMJ Open 2025;15:e090012 (https://doi.org/10.1136/bmjopen-2024-090012).
21. Arienzo, A., Cellitti, V., Ferrante, V. et al. A new point-of-care test for the rapid detection of urinary tract infections. Eur J Clin Microbiol Infect Dis. 2020;39:325–332 (https://doi.org/10.1007/s10096-019-03728-3).
22. Leuthner K. Approaching treatment for complicated UTIs. Contagion Live. 2023; Jun 1 (https://www.contagionlive.com/view/approaching-treatment-for-complicated-utis).
23. Vannice K, MacLennan CA, Long J, Steele AD. Open Forum Infect Dis. 2024;11(Supplement 1):S1–S5 (https://doi.org/10.1093/ofid/ofad586).
24. Héma A, Sermé SS, Sawadogo J, Diarra A, Barry A, Ouédraogo AZ, et al. Contribution of the rapid LAMP-based diagnostic test (RLDT) to the evaluation of enterotoxigenic Escherichia coli (ETEC) and Shigella in childhood diarrhea in the peri-urban area of Ouagadougou, Burkina Faso. Microorganisms. 2023;11(*11*):2809 (https://doi.org/10.3390/microorganisms11112809).
25. Wolcott R. Biofilm and catheter-related bloodstream infections. Br J Nurs. 2021;30(*8*):423–31 (https://doi.org/10.12968/bjon.2021.30.8.s4).
26. Rottier W, Seidelman J, Wouthuyzen-Bakker M. Antimicrobial treatment of patients with a periprosthetic joint infection: basic principles. Arthroplasty. 2023;5(*1*):10 (https://doi.org/10.1186/s42836-023-00169-4).
27. Antimicrobial resistance threats in the United States, 2021–2022. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2022 (https://www.cdc.gov/antimicrobial-resistance/data-research/threats/update-2022.html).
28. Global road map on defeating meningitis by 2030. In: Resolutions and decisions. Seventy-third World Health Assembly. Geneva: World Health Organization; 2020 (https://apps.who.int/gb/ebwha/pdf_files/WHA73-REC1/A73_REC1-en.pdf).
29. Defeating meningitis by 2030: a global road map. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/342010).

(All references were accessed on 10 November 2025).

World Health Organization
20 Avenue Appia, 1211 Geneva
Switzerland